

Monostotic fibrous dysplasia of the lumbar spine

Agbessi Martin Avimadje, Philippe Goupille, Djamila Zerkak,
Géraldine Begnard, Juliette Brunais-Besse, Jean-Pierre Valat

Rheumatology Department, Trousseau Teaching Hospital, 37044 Tours cedex, France

(Submitted for publication August 5, 1999; accepted in revised form October 20, 1999)

Summary – Monostotic fibrous dysplasia is exceedingly rare. We report a case in a 61-year-old woman with a history of recurrent low back pain and sciatica since 35 years of age. While walking, she suddenly experienced pain in her right thigh. The pain spread gradually to the buttock and calf on the same side, becoming increasingly severe. The time pattern was mechanical, with exacerbation during straining. Paresthesia developed over the dorsal aspect of the right foot. Nonsteroidal antiinflammatory drugs were ineffective. Radiographs of the spine showed an expansile and heterogeneous lesion in the body of L2. Hyperactivity of L3 and L4 was seen on the bone scan. Computed tomography demonstrated heterogeneity of L2, L3, and L4, as well as hypertrophy of the neural arch of L3 and of the right posterior lamina and spinous process of L4. Alterations in L2, L3, and L4 were noted on the magnetic resonance imaging study, which showed no evidence of epidural involvement. Laboratory tests were normal. A surgical biopsy of L3 established the diagnosis of fibrous dysplasia. Since the seminal description of fibrous dysplasia in 1891, only 21 cases of monostotic spinal involvement have been published. The spinal lesions can remain clinically silent or cause spinal pain with or without neurological symptoms. Radiographic findings are variable (heterogeneity, osteolysis, expansion without cortical violation or soft tissue involvement). Calcium and phosphate levels are normal. The diagnosis depends on examination of a vertebral biopsy specimen.)

Joint Bone Spine 2000 ; 67 (1) : 65-70. © 2000 Éditions scientifiques et médicales Elsevier SAS.

fibrous dysplasia / lumbar spine

Fibrous dysplasia of bone, or Jaffé-Lichtenstein disease, is a benign bone tumor characterized by proliferation of connective fibrous tissue containing trabeculae of woven bone [1]. Fractures and deformities can occur [2]. Spinal involvement is rare, particularly in monostotic forms, but carries a risk of neurological compromise. We report a case of monostotic fibrous dysplasia of the lumbar spine.

CASE-REPORT

A 61-year-old woman was admitted to our rheumatology department in March 1992 for evaluation and treatment of increasingly severe chronic sciatica. In February 1991, while

walking, she suddenly experienced pain at the anterior aspect of her right thigh. Over the next month the pain took on a mechanical pattern, became increasingly severe, and spread gradually to the right buttock and to the lateral aspect of the right thigh and calf. Straining exacerbated the pain. Paresthesia developed over the dorsum of the right foot. Neither nonsteroidal antiinflammatory drugs nor analgesics provided relief. She had a history of back pain during adolescence and of about four episodes per year of low back pain and sciatica since 35 years of age. At admission, she was in good general health, and no point tenderness was found at the right thigh. Range of motion of the lumbar spine was normal. Tenderness to pressure was found at L4-L5 and skin roll over the right iliac crest elicited a burning sensation. Both hips had a full and pain-free range of

motion. The straight leg-raising test was negative on both sides. The knee jerks were present and symmetric but weak, and both ankle jerks were absent. Paresthesia was noted over the great toe of the right foot. Sphincter function was normal. Plain radiographs of the spine and pelvis (June 1991) demonstrated a heterogeneous and expansile lesion in the body of L2 (*figure 1*). Hyperactivity was seen from L3 to L5 on a bone scan done in August 1991; no other foci were visible. Computed tomography demonstrated heterogeneity of the bodies of L2, L3, and L4, as well as hypertrophy of the L3 neural arch predominating on the right; at L4, the right half of the neural arch was heterogeneous and the right lamina and spinous process were hypertrophied (*figure 2*). The overall shape of the vertebrae, spinal canal diameter, cortices, and soft tissues were normal. A magnetic resonance study done in October 1991 showed alterations in L2, L3, and L4 without evidence of epidural involvement. The erythrocyte sedimentation rate was 10 mm/h and the C-reactive protein level was 1.2 mg/L. The alkaline phosphatase level was normal, the serum calcium level was at the lower limit of normal (2.25 mmol/L), and the serum phosphate level was at the upper limit of normal (1.28 mmol/L). A surgical biopsy of L3 was performed. The specimen was examined without prior decalcification. The histologic pattern was suggestive of fibrous dysplasia: small trabeculae of very poorly mineralized woven bone separated from one another by fibrous tissue containing evenly distributed fibroblasts were seen, with no noticeable osteoblastic activity or resorption. The patient was lost to follow-up until October 1994, when she again started experiencing pain in her right lower limb, down to the sole of the foot, with paresthesia in the second to fifth toes. She also reported intermittent pain in the back of her left thigh down to the knee. The pain was more severe than previously and became increasingly incapacitating. Epidural glucocorticoid injections and traction of the lumbar spine were ineffective. An intravenous infusion of pamidronate (60 mg/day for three days) produced a noticeable improvement. One year later, the only symptom was moderately severe low back pain, and there was no evidence of worsening of the lesions on radiographs of the lumbar spine.

DISCUSSION

Fibrous dysplasia accounts for 2.5% of all bone lesions and 7% of benign bone tumors [3]. The disease can be polyostotic or monostotic. McCune Albright syndrome is a variety of fibrous dysplasia in which polyostotic lesions are accompanied with precocious sexual development and café-au-lait spots [4]. The spine is involved in only 4% to 14% of polyostotic forms [5, 6]. Only 21 cases of monostotic spinal involvement have been published [5, 7-24]; there were ten men and nine women, and in two cases the sex was not specified [24]. Our patient was a woman. The first clinical



Figure 1. Plain radiograph: expansion and heterogeneity of the body of L2.

symptoms of fibrous dysplasia usually occur between five and 20 years of age, although some forms are silent until adulthood [2, 8]. Of the 21 patients with monostotic spinal disease, only three experienced

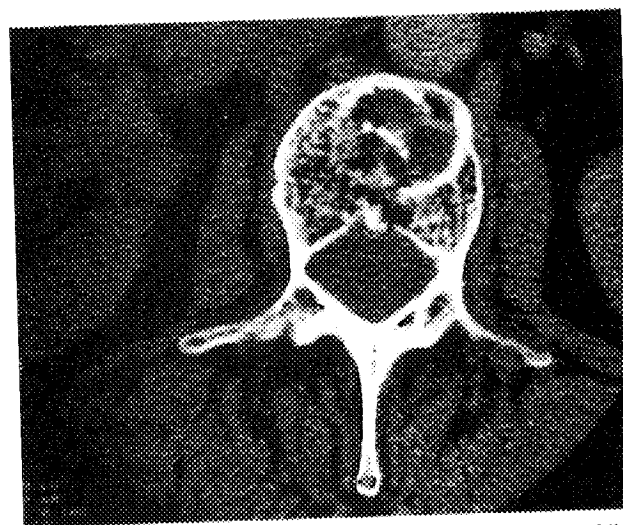


Figure 2. Computed tomography: heterogeneous appearance of the body of L2.

symptoms before 20 years of age [8, 18, 23]; one was older than 50 years at the time of the first symptoms, and our patient was 61.

Pathophysiology

Lichtenstein described fibrous dysplasia in 1938 as "a disturbance in the development of bone-forming mesenchyme caused by fibrous tissue containing trabeculae of scantily calcified primitive bone" [1]. Since then, convincing evidence that the disease is in large part genetic has been obtained [25-28]. The affected bone demonstrates a mosaic mutation at position 201 of exon 8 of the Gs protein subunit (substitution of histidine or cysteine for arginine). This mutation activates the enzyme adenylate cyclase, thus causing increased cell division and inappropriate cell differentiation. The result is overproduction of haphazardly organized bone matrix.

Sites of involvement [2, 5, 8, 29, 30]

The bone lesions are usually limited to one side of the body; when the lesions are bilateral, they usually predominate on one side, in one or both limbs. Of the patients with monostotic spinal disease, 9 had involvement of the lumbar spine, 8 of the cervical spine, and 5 of the thoracic spine (*table I*). The body and neural arch were involved in 14 cases, usually with more severe lesions on the right side [5, 9-12, 15, 16, 18-23]. Our patient had lesions in the bodies of L2, L3, and L4 and in the neural arch of L3 and L4, with predominant involvement of the right side.

Clinical manifestations

The disease, particularly in its monostotic variety, can remain clinically silent far into adulthood, being revealed only by radiographs done for another reason [30]. One-third of the published cases of monostotic spinal involvement were diagnosed after an injury [9, 10, 19, 20-23]. Symptoms in the other cases consisted of low back pain [5, 7, 8, 15, 23], back pain [16, 17], neck pain [19, 20, 22], peripheral neurological manifestations or spinal cord compression [9-11, 14, 18, 20, 21].

Laboratory tests

One-third of the patients with monostotic spinal disease had high levels of serum alkaline phosphatase and urinary hydroxyproline, with normal calcium

and phosphate levels [2, 19]. The urinary excretion of the C-terminal peptide of type I collagen may reflect disease activity [3].

Imaging studies

Plain radiographs of the spine can show a variety of abnormalities, including osteolysis without cortical violation [8, 9, 16, 17, 19, 21, 31], a radiolucency [5, 24], expansion with widening of the pedicle [10-12, 14], a patchy appearance with granular striations of the vertebral body suggestive of an angioma [11], or a ground-glass appearance [14]. Our patient had expansile and heterogeneous lesions without cortical involvement. The bone scan typically demonstrates hyperactivity in one or more vertebrae [12, 16-20, 23]; false negatives can occur, however: in a study of 80 lesions with radiographic abnormalities consisting in a ground-glass appearance ($n = 30$), a cyst ($n = 29$) or a deformity ($n = 21$). Scintigraphic hyperactivity was seen in 28 cases (93%), 23 cases (79%) and 18 cases (86%), respectively [32]. Computed tomography shows a heterogeneous lesion or osteolysis without cortical violation; this investigation is useful to look for soft tissue involvement or spinal canal changes and to evaluate the risk of spinal cord compression [9, 10, 12, 18, 19]. Magnetic resonance imaging shows low signal on T1-weighted images in 18% of cases, high signal on T2-weighted images in 60%; in 18% of cases, no signal abnormalities are found [33-35].

Histology [2, 5, 8, 29, 30, 36]

A bone biopsy must be performed to establish the diagnosis in monostotic forms without highly typical radiographic changes and to rule out malignant transformation in patients with recent-onset of pain or with radiological modifications in a known lesion. Histology is not indispensable in polyostotic forms. The cortex is always intact, albeit thin and spongy. The center of the lesion is composed of compact, firm, whitish tissue that is rubbery or gritty to the touch and usually contains few blood vessels (except in hemorrhagic forms); cystic cavities and, in some cases, cartilaginous lobules are visible. Under the microscope, haphazardly distributed trabeculae of woven bone are seen; the bone is not organized in lamellae, and there are no osteoblasts at the periphery of the lesion. These characteristics are strongly suggestive of fibrous dysplasia. In doubtful cases, a study under polarized light demonstrates typical woven bone.

Table 1. Cases of monostotic fibrous dysplasia of the spine.

<i>Authors</i>	<i>Daniluk</i>	<i>Ehara</i>	<i>Harris</i>	<i>Hu</i>	<i>Kahn</i>	<i>Ledoux-Lebard</i>	<i>Nabarro</i>	<i>Nigrisoli</i>	<i>Nishiura</i>	<i>Nyul-Toth</i>
Age (years)	28	19	42	41	23	58	46	36	37	26
Sex	F	M	M	M	M	F	F	F	M	M
Time to diagnosis	10 years	NS NS	NS	6 months	acute	6 years	6 weeks	3 years	6 months	3 years
Neurological manifestations	No	No NS	No	No	Sensory loss in the right leg	Flaccid paraplegia and sphincter dysfunction	No	No	Grasping-brisk reflexes	No
History of injury	No	NS NS	No	Cervical spine	Yes	No	No	No	No	No
Site(s) involved	L4 R	C1 L3 (a)	L4 R (ap)	C2 R (ap)	L3 R (ap)	L1 (ap)	T7 R (ap)	L3 (a)	C1,C2 (a)	L2 L3 (ap)
Treatment	Excision	NS NS	Biopsy	Biopsy fixation	Biopsy fixation	Biopsy decompression	Excision fixation	Curettage fusion	Excision fusion	Biopsy fusion
Outcome	No pain	NS NS	Pain after 4 years	Fusion after 30 months	Fusion after 9 months mild pain	NS	Fusion after 6 months pain free	Pain after 6 months	Fusion after 1 year	Pain-free after 1 year
<i>Authors</i>	<i>Oba</i>	<i>Penrod</i>	<i>Prybylski</i>	<i>Resnik</i>	<i>Rosenblum</i>	<i>Rosendal-Jensen</i>	<i>Schlumberger</i>	<i>Troop</i>	<i>Wright</i>	<i>Our patient</i>
Age (years)	48	40	12	27	20	35	20	12	NS NS	60
Sex	F	F	M	F	M	F	M	F	NS NS	F
Time to diagnosis	Acute	9 months	2 weeks	Acute	Acute	1 year	11 months	Acute	NS NS	1 year
Neurological manifestations	No	No	Urinary retention and pyramidal syndrome	No	Decreased tricipital	Sensory disorders in the left upper limb	No	No	NS NS	No
History of injury	No	No	No	Cervical spine	Cervical spine	Fall on a flight of steps	Cervical spine	Fall	NS NS	No
Site(s) involved	T10 G (ap)	T3 D (ap)	T5 D (ap)	C6 D (ap)	T1 D (ap)	C4 G (ap)	C4 D (ap)	L3 D (ap)	C2 C5 (p)	L2-L4 D (ap)
Treatment	Excision	Excision	Excision-fixation	Biopsy	Excision-halo traction	Curettage	Biopsy	Excision-fusion	NS NS	Biopsy IV-pamidronate
Outcome	Pain-free after 3 years	NS	Pain free	NS	Pain-free after 3 months	Pain-free	NS	Pain-free after 3 years	NS NS	Pain improved after 1 year

NS: not significant; ap: involvement of both anterior and posterior part of vertebrae; a: involvement of only anterior part; p: involvement of only posterior part; na: not available.

Course and complications

In the absence of treatment, the lesions are often stable in adulthood [29], although spreading occurs in some cases [5, 30, 37]. Markedly vascular lesions can increase in size as a result of bleeding or cyst formation; this can result in deformities or, at the spine, in neurological compromise [38, 39]. Among patients with polyostotic disease, 85% develop pathological fractures [2, 30]. Sarcomatous transformation (osteosarcoma, fibrosarcoma, chondrosarcoma) occurs in 0.4% to 6.7% of cases [3, 7, 40-43] and is most common in men and between 30 and 40 years of age [7, 40, 42]. Radiation therapy increases the risk of malignancy and is consequently contraindicated [42]. Furthermore, during follow-up, radiographs should be restricted to the evaluation of painful sites [42].

Treatment

Watchful waiting and surgery were the only therapeutic alternatives until a few years ago, when pamidronate was found to be beneficial. A number of studies [43-47] have allowed to define criteria for pamidronate therapy in fibrous dysplasia. Intravenous pamidronate infusions should be given in a dosage of 60 mg/day in adults and 1 mg/kg/day in children, on three consecutive days every six months for two years. The infusions can then be spaced further apart depending on the clinical response. Supplemental calcium (1 g/d) and vitamin D (800 IU/d) should be given. Pain should be evaluated every six months, radiographs taken as needed, and laboratory tests performed (serum calcium, phosphate, and alkaline phosphatase). Pamidronate therapy consistently provides pain relief, and radiographic improvements are visible after 18 months in 50% of cases. We are not aware of any published cases of isolated spinal involvement treated by pamidronate. The single pamidronate infusion given to our patient seems to have been effective on the pain and was not followed by any further radiological progression.

CONCLUSION

Chronic low back pain with or without neurological symptoms can be a manifestation of lumbar spine involvement by fibrous dysplasia. Monostotic spinal involvement is exceedingly rare but can be suspected in patients with osteolysis and/or expansion of a vertebra without cortical violation; the diagnosis depends on obtaining a biopsy specimen. In polyostotic forms,

the onset at an early age and the presence of typical radiological changes in other bones can suffice to establish the diagnosis. A number of studies have allowed to define criteria for pamidronate therapy in fibrous dysplasia. Pamidronate may be valuable for preventing the occurrence of neurological compromise in patients with spinal involvement.

REFERENCES

1. Lichtenstein L, Jaffe HL. Fibrous dysplasia of bone. A condition affecting one, several or many bones, the graver cases of which may present abnormal pigmentation of skin, premature sexual development, hyperthyroidism or still other extra-skeletal abnormalities. *Arch Pathol* 1938 ; 33 : 777-816.
2. Laredo JD, Champsaur P, Hamze B. Dysplasie fibreuse des os et dysplasie ostéofibreuse. Mise au point. *Ann Radiol* 1995 ; 38 : 225-36.
3. Chapurlat R. Dysplasie fibreuse des os et biphosphonates. *La Lettre du Rhumatologue* 1998 ; 246 : 25-8.
4. MacCune O, Bruch H. Osteodystrophia fibrosa. Report of a case in which the condition was combined with precocious puberty, pathologic pigmentation of the skin and hyperthyroidism, with a review of the literature. *Am J Dis Child* 1937 ; 54 : 806-48.
5. Harris WH, Dudley HR, Barry RJ. The natural history of fibrous dysplasia. *J Bone Joint Surg* 1962 ; 44A : 207-33.
6. Mirra JM, ed. Bone tumors, diagnosis and treatment. Philadelphia : Lippincott ; 1980. p. 122-37.
7. Daniluk A, Witwicki T. A case of fibrous dysplasia of the spine. *Chir Narz Ruchu Ortop Pol* 1979 ; 44 : 165-7.
8. Ehara S, Kattapuram SV, Rosenberg AE. Fibrous dysplasia of the spine. *Spine* 1992 ; 17 : 977-9.
9. Hu SS, Healey JH, Huvo AG. Fibrous dysplasia of the second cervical vertebra. *J Bone Joint Surg* 1990 ; 72A : 781-3.
10. Kahn A, Rosenberg PS. Monostotic fibrous dysplasia of the lumbar spine. *Spine* 1988 ; 13 : 592-4.
11. Ledoux-Lebard G, Soulquin C. Les localisations vertébrales de la dysplasie fibreuse des os ou maladie de Jaffé-Lichtenstein. *J Radiol* 1953 ; 34 : 349-52.
12. Nabarro MN, Giblin PE. Monostotic fibrous dysplasia of the thoracic spine. *Spine* 1994 ; 19 : 463-5.
13. Nigrisoli M. Monostotic fibrous dysplasia of the spine: case report. *Ital J Orthop Traumatol* 1987 ; 13 : 273-8.
14. Nishiura I, Koyama T, Takayama S. Fibrous dysplasia of the cervical spine with atlanto-axial dislocation. *Neurochirurgia* 1992 ; 35 : 123-6.
15. Nyul-Toth P, Joos M. Über die Wirbelmanifestation der fibrosen Dysplasie. *Fortschr Geb Röntgenstrahlen nuklearmed Ergänzungsbd* 1974 ; 120 : 744-7.
16. Oba M, Nakagami W, Maeda M, Kobayashi K. Symptomatic monostotic fibrous dysplasia of the thoracic spine. *Spine* 1998 ; 23 : 741-3.
17. Penrod BJ, Haramati N, Frager D, Dorfman HD. A 40-year-old woman with back pain. *Clin Imaging* 1996 ; 20 : 143-6.
18. Przybylski GJ, Pllack IF, Ward WT. Monostotic fibrous dysplasia of the thoracic spine. *Spine* 1996 ; 21 : 860-5.
19. Resnik CS, Lininger JR. Monostotic fibrous dysplasia of the cervical spine: a case report. *Radiology* 1984 ; 151 : 49-50.

20. Rosenblum B, Overby C, Levine M, Handler M, Sprecher S. Monostotic fibrous dysplasia of the thoracic spine. *Spine* 1987 ; 12 : 939-42.
21. Rosendal-Jensen SV. Fibrous dysplasia of the vertebral column. *Acta Chir Scand* 1956 ; 111 : 490-4.
22. Schlumberger HG. Fibrous dysplasia of single bones. *Military Surgeon* 1946 ; 99 : 504-27.
23. Troop JK, Herring JA. Monostotic fibrous dysplasia of the lumbar spine: case report and review of the literature. *J Pediatr Orthop* 1988 ; 8 : 599-601.
24. Wright JFC, Stoker DJ. Fibrous dysplasia of the spine. *Clin Radiol* 1988 ; 39 : 523-7.
25. Candelieri GA, Roughley PJ, Glorieux FH. Polymerase chain reaction-based technique for the selective enrichment and analysis of mosaic arg 201 mutations in Gs α from patients with fibrous dysplasia of bone. *Bone* 1997 ; 21 : 201-6.
26. Shenker A, Chanson P, Weinstein LS. Osteoblastic cells derived from isolated lesions of fibrous dysplasia contain activating somatic mutations of the Gs α gene. *Hum Mol Genet* 1995 ; 4 : 11675-6.
27. Shenker A, Weinstein LS, Sweet DE. An activating Gs α mutation is present in fibrous dysplasia of bone in the McCune-Albright syndrome. *J Clin Endocrinol Metab* 1994 ; 79 : 750-5.
28. Marie PJ, de Pollak C, Chanson P. Increased proliferation of osteoblastic cells expressing the activating Gs α mutation in monostotic and polyostotic fibrous dysplasia. *Am J Pathol* 1997 ; 150 : 1059-69.
29. Languepin A. Dysplasie fibreuse et fibrome ossifiant. In: Tomeno B, Forest M éd. *Les tumeurs osseuses de l'appareil locomoteur*. Paris: Laboratoires UNICET; 1987.
30. Henry A. Monostotic fibrous dysplasia. *J Bone Joint Surg* 1969 ; 51B : 300-6.
31. Brumsen C, Hamdy NAT, Papapoulos SE. Long-term effects of biphosphonates on the growing skeleton. *Medicine* 1997 ; 76 : 266-83.
32. Machida K, Matika K, Nishikawa J. Scintigraphic manifestations of fibrous dysplasia. *Clin Nucl Med* 1986 ; 11 : 426-9.
33. Inamo Y, Hanawa Y, Kin H, Okuni M. Findings on magnetic resonance imaging of the spine and femur in a case of McCune-Albright syndrome. *Pediatr Radiol* 1993 ; 23 : 15-8.
34. Jee WH, Choi KH, Choe BY, Park JM, Shinn BH. Fibrous dysplasia: MR imaging characteristics with radiopathologic correlation. *AJR* 1996 ; 167 : 1523-7.
35. Utz JA, Kransdorf MJ, Jelinek JS, Moser RP Jr, Berrey BH. MR appearance of fibrous dysplasia. *J Comput Assist Tomogr* 1989 ; 13 : 845-51.
36. Bianco P, Robey PG. An animal model of fibrous dysplasia. *Mom Med Today* 1999 ; 5 : 322-3.
37. Firat D, Stutzman L. Fibrous dysplasia of the bone. Review of twenty-four cases. *Am J Med* 1968 ; 44 : 421-9.
38. Smith MD, Bohlman HH, Gideonse N. Fibrous dysplasia of the cervical spine: a fatal complication of treatment. *J Bone Joint Surg* 1990 ; 72A : 1254-8.
39. Stirrat AN, Fyfe IS, Fisher CJ. Fibrous dysplasia of the axis. *Spine* 1989 ; 14 : 243-5.
40. Yabut SM, Kenan S, Sissons HA, Lewis MM. Malignant transformation of fibrous dysplasia. *Clin Orthop* 1988 ; 228 : 281-9.
41. Yalniz E, Er T, Özyilmaz F. Fibrous dysplasia of the spine with sarcomatous transformation: a case report and review of the literature. *Eur Spine J* 1995 ; 4 : 372-4.
42. Ruggieri P, Sim FH, Bond JR, Uni KK. Malignancies in fibrous dysplasia. *Cancer* 1994 ; 73 : 1411-24.
43. Bone H, Cody D. Intravenous pamidronate treatment of fibrous dysplasia of bone. *J Bone Miner Res* 1996 ; 11 : S249.
44. Chapurlat R, Delmas PD, Meunier PJ. Suivi prolongé de 28 patients atteints de dysplasie fibreuse traités par pamidronate [abstract]. *Rev Rhum [Ed Fr]* 1998 ; 65 : 245S.
45. Chapurlat RD, Delmas PD, Liens D, Meunier PJ. Long-term effects of intravenous pamidronate in fibrous dysplasia of bone. *J Bone Miner Res* 1997 ; 12 : 1746-52.
46. Liens D, Delmas PD, Meunier PJ. Long-term effects of intravenous pamidronate in fibrous dysplasia of bone. *Lancet* 1994 ; 343 : 953-4.
47. Weinstein RS. Long-term aminobiphosphonate treatment of fibrous dysplasia: spectacular increase in bone density. *J Bone Min Res* 1997 ; 12 : 1314-5.